A. BACKGROUND AND RATIONALE OF THE TRIAL

1. **Provide the following information about the proposed study: the title, the investigators, address, phone and fax numbers.**

Title:	"Phase II Study of Immunotherapy of Metastatic Cancer by Direct Gene Transfer"
Principal Investigators:	Gary J. Nabel, M.D., Ph.D. Alfred E. Chang, M.D.
Institution:	University of Michigan Medical Center Howard Hughes Medical Institute 1150 West Medical Center Drive 4510 MSRB I Ann Arbor, MI 48109-0650 (313) 747-4798 (313) 747-4730 Fax

2. **Provide a brief rationale for the clinical trial.**
The proposed Phase II study represents further development of the HLA-B7 plasmid DNA/Lipid complex, VCL-1005 ("Allovectin-7"), for the immunotherapy of cancer. This protocol builds on the safety and biological activity results obtained from Phase I studies which are nearly completed.

A summary review of clinical and laboratory data collected from 80% of the planned patient enrollment is provided in section 3.0 of the proposed clinical protocol, submitted with this cover sheet.

As in the Phase I protocols, we will introduce the gene encoding the allogeneic human transplantation antigen, HLA-B7 heavy chain, and a gene-encoding β2 microglobulin, into tumors *in vivo*.

The objectives of the proposed Phase II protocol are:

a) To estimate the shrinkage and duration of shrinkage in the injected lesions(s) in patients with advanced cancers in response to therapy with intralesional Allovectin-7 (HLA-B 7, β2 microglobulin/DMRIE/DOPE complex).
b) To estimate the overall response rate and duration of response in patients receiving Allovectin-7.
c) To evaluate the toxicity of intralesional Allovectin-7 in patients with advanced metastatic cancer.
d) To assess the relationship of patient response to expression of HLA-B7 after treatment (PCR and immunohistochemistry will be used to confirm gene transfer).

B. SIMILARITY TO OTHER RAC-APPROVED PROTOCOLS

1. **Is the proposed study identical to another RAC-approved protocol except that the study will be performed at a satellite institution? If so, . . .**
While the proposed Phase II protocol is very similar to another RAC approved protocol, it is not identical. Modest differences are described in B.2. below.